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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO:	CONFIRMATION NO.
08/758,033	11/27/1996	GARY L. CLAYMAN	INGN:022	5378

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	39

DATE MAILED: 12/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/758,033	CLAYMAN, GARY L.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *February 19, 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16-32,36 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,16-32,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This application claims benefit to provisional application 60/007,810, filed November 30, 1995.

The decision by the Board of Patent Appeals and Interferences mailed March 20, 2002, paper number 37, has been entered. As indicated the rejections of record have been vacated and remanded to the Examiner for further action. See paper number 37, page 3.

In addition to the issues raised by in comments by the Board, a new search of pending applications and the relevant art has provided a new basis of rejection.

Claims 1-14, 16-20, 26-32, 36 and 37 are pending and currently under examination.

Response to Amendment

As indicated in the decision by the Board of Patent Appeals and Interferences, the declaration of Dr. Gary Clayman filed on November 18, 1999, paper number 25, under 37 CFR 1.131 has been considered but is ineffective to overcome the Katayose and Srivastava references. The declaration therefore fails to satisfy the express terms of rule 131 (page 9), and does not facially inadequate to antedate the references (bridging pages 12-13). Further, the Board has indicated that upon analysis of the Katayose and Srivastava references it appears that they are

"very relevant to the issue of the patentability of the instant claims under 35 U.S.C. 103 (page 13).

Because the Examiner erred in withdrawing the Katayose and Srivastava references that the Board indicated to be relevant, and the references qualify as prior art under 35 U.S.C. 102(a), a new rejection considering these references is being made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-14, 16-20, 26-32, 36 and 37 are provisionally rejected under the judicially created doctrine of double patenting over claims 26-88 of copending Application No. 09/968,958. This is a provisional double patenting rejection since the conflicting claims have not yet been patented. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

In the instant case, the method set forth in claim 1 of the instant application is essentially the same as that set forth in claim 58 of '958. Further, it is noted that claim 26 of application '958 encompasses essentially the same invention as encompassed by claims 1 and 12 of '033. Dependent claims in each application set forth specific types and amounts of vectors, specific types of cancers, and specific times of administration that set forth inventions which are essentially the same in breadth between both applications.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-9, 13, 14, 16-20 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Liu *et al.* (IDS Reference).

Liu *et al.* teach a method of reducing tumor burden in a mouse following the administration of an adenoviral vector encoding a wild-type p53 polypeptide. Liu *et al.* reduce to practice specifically administration to a squamous cell carcinoma in the model system used, however teach that the methods could be applied to other types of cancers. The adenoviral vector used in the methods is deleted of the E1 region and has a CMV promoter for expression of the p53 inserted therein. The vector is delivered surgically to a revealed tumor in 100ul volumes in increasing log increments up to 10^{12} PFU to test efficacy.

Claims 1-9, 13, 14, 16-20 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Clayman *et al.* (IDS Reference).

Clayman *et al.* teach a method of reducing tumor burden in a mouse following the administration of an adenoviral vector encoding a wild-type p53 polypeptide. More specifically, Clayman *et al.* Cite and teach that the methods disclosed are similar to those set forth in Liu *et al.* (page 2, second column- as discussed above). Clayman *et al.* reduce to practice specifically administration to a squamous cell carcinoma in the model system used, however teach that the methods could be applied to other types of cancers. Clayman *et al.* teaches that the endogenous p53 in the caner cell to be treated can be normal or mutated. The adenoviral vector used in the methods is deleted of the E1 region and has a CMV promoter for expression of the p53 inserted therein. The vector is delivered surgically to a revealed tumor in 100ul volumes in increasing log increments up to 10^{12} PFU to test efficacy of the vector in the disclosed methods.

Claims 1-14, 16-20, 26-32, 36 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Roth *et al.* (5,747,469 or 6,017,524).

Roth *et al.* teach a method of treating a tumor by killing the cells of the tumor through the expression of p53 (see claim 1 of '469). The vector can be deliver by a variety of vectors including adenoviral vectors (see claims 2 and 15 of '469), and in conjunction with known chemotherapeutic agents and protocols normally used alone in the treatment of tumors (see claims 3-13 of '469). Roth *et al.* teach to optimize deliver of specific a specific vector for

different PFU and volumes (see claims 16-18 and 49 of '469) and in part for the use of different types of promoters such as the CMV promoter (see claims 23 and 24 of '469). In the course of successfully practicing the claimed methods, Roth *et al.* teach that for effective treatment multiple times and multiple sites of delivery may be necessary to affect the entire tumor or the entire bed from which the tumor has been removed.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-14, 16-20, 26-32, 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clayman *et al.* and Liu *et al.* in view of Zhang *et al.*

The teachings of Clayman *et al.* and Liu *et al.* are summarized above as they apply to claims 1-9, 13, 14, 16-20 and 36. Briefly, both Liu *et al.* and Clayman *et al.* teach a method of reducing tumor burden in a mouse following the administration of an adenoviral vector encoding a wild-type p53 polypeptide. Each reduce to practice specifically administration to a squamous cell carcinoma in the model system used, however teach that the methods could be applied to other types of cancers. The adenoviral vector used in the methods is deleted of the E1 region

and has a CMV promoter for expression of the p53 inserted therein. The vector is delivered surgically to a revealed tumor in 100ul volumes in increasing log increments up to 10^{12} PFU to test efficacy. However, Clayman *et al.* and Liu *et al.* do not specifically teach to the specific volumes or spacing for the injections, nor to perform treatment of cancer with wild-type p53 with other well established methods of cancer treatment. Initially, it is noted that Liu *et al.* and Clayman *et al.* teach to use surgery to reveal the tumor being treated and to aid in the delivery of the vectors. In light of this, it would be obvious to one of ordinary skill in the art based on the size and location of the cancer, to treat the cancer with multiple injections and various volumes consistent with the size and shape of the cancer in the subject in order to fully transfect the cancer to be treated. In addition to the treatment by gene therapy protocols, Zhang *et al.* teach that gene therapy can successfully be combined with gene therapy to enhance the treatment of cancer. At the time of the claimed invention, operable tumors and cancer were either first treated with chemotherapeutic agents to reduce the size of the tumor, and/or subsequent to removal to treat the residual microscopic cancer that was left in the subject. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the use of conventional methods of cancer treatment such a s surgery and the use of chemotherapeutics with methods of gene therapy as taught by Zhang *et al.* One having ordinary skill in the art would have been motivated to combine complementing methods of cancer treatment in order to completely treat the cancer in a subject. Each of the methods themselves are capable alone of providing treatment therefore, there would have been a reasonable

expectation of success to combine the complementing methods for a more extensive and complete treatment of cancer.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Claims 1-14, 16-20, 26-32, 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srivastava *et al.*, Cajot *et al.*, Katayose *et al.*, Will *et al.*, Liu *et al.* and Zhang *et al.*

Srivastava *et al.* teach a method of inhibiting the growth of wild-type p53 expressing LNCaP cells with adenoviral vectors encoding and expressing p53. Further Srivastava *et al.* teach that treatment with such vectors can be practiced *in vivo*. Cajot *et al.* and Katayose *et al.* provide in vitro evidence that analogous methods work in other transformed cells types reducing to practice inhibition of Hut292DM cells and MCF-1 cells. Similar to the teaching of Srivastava *et al.* Will *et al.* teach the repetitive delivery of adenoviral vectors encoding wild-type p53 for the inhibition of tumor growth in an animal. Will *et al.* demonstrate that method can be successfully applied to a variety of tumor types and that different levels of treatment could be achieved with different multiplicity of infection (figure 4). In addition, Will *et al.* teach that combination of the treatment with p53 expressing vectors with conventional cancer treatments may increase the tumor cell susceptibility to radiation or chemotherapy commonly used. Zhang *et al.* specifically teach that gene therapy can be complemented by conventional well known methods for the treatment of cancer. Therefore, given the teachings above it would have been *prima facie*

obvious to one having ordinary skill in the art at the time the invention was made to combine known conventional methods for the treatment of cancer with complementing methods of gene therapy treatment. Each Srivastava *et al.*, Cajot *et al.*, Katayose *et al.*, Will *et al.*, Liu *et al.* and Zhang *et al.* represent analogous art for the treatment of cancer providing clear and specific motivation to one of ordinary skill in the art for the use of p53 expressing adenoviral vectors to inhibit tumor cell growth and the use of such gene therapy to complement conventional cancer treatment methods practiced in the art. There would have been a reasonable expectation of success to combine the method of gene therapy and conventional cancer treatment given that the methods themselves alone provide treatment by inhibiting growth or killing the cancer cells in a subject.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

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